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# Main Figures: 7

# Supplementary Figures: 3

# Supplementary Tables: 7

# Supplementary Videos: 0

## Reporting Checklist for Nature Neuroscience

This checklist is used to ensure good reporting standards and to improve the reproducibility of published results. For more information, please read [Reporting Life Sciences Research](#).

Please note that in the event of publication, it is mandatory that authors include all relevant methodological and statistical information in the manuscript.

### ► Statistics reporting, by figure

- Please specify the following information for each panel reporting quantitative data, and where each item is reported (section, e.g. Results, & paragraph number).
- Each figure legend should ideally contain an exact sample size (n) for each experimental group/condition, where n is an exact number and not a range, a clear definition of how n is defined (for example x cells from x slices from x animals from x litters, collected over x days), a description of the statistical test used, the results of the tests, any descriptive statistics and clearly defined error bars if applicable.
- For any experiments using custom statistics, please indicate the test used and stats obtained for each experiment.
- Each figure legend should include a statement of how many times the experiment shown was replicated in the lab; the details of sample collection should be sufficiently clear so that the replicability of the experiment is obvious to the reader.
- For experiments reported in the text but not in the figures, please use the paragraph number instead of the figure number.

**Note:** Mean and standard deviation are not appropriate on small samples, and plotting independent data points is usually more informative. When technical replicates are reported, error and significance measures reflect the experimental variability and not the variability of the biological process; it is misleading not to state this clearly.

	TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
example 1a	one-way ANOVA	Fig. legend	9, 9, 10, 15	mice from at least 3 litters/group	Methods para 8	error bars are mean +/- SEM	Fig. legend	p = 0.044	Fig. legend	F(3, 36) = 2.97	Fig. legend
example results, para 6	unpaired t-test	Results para 6	15	slices from 10 mice	Results para 6	error bars are mean +/- SEM	Results para 6	p = 0.0006	Results para 6	t(28) = 2.808	Results para 6

	TEST USED			n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
+ -	1	hierarchical clustering (Pearson's linear dissimilarity measure)	"cis-eQTL signals cluster in biologically meaningful ways", para 1	130	all cerebellar cortex samples	Online Methods "Collection and dissection of post-mortem human brain tissues"	heatmap coloured by (a) absolute z scores; (b) mean expression within each brain region	Figure legend	NA	NA	NA	NA
+ -	2a	None	NA	134	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Number of cis-eQTL signals which were seen in N brain regions (and the proportion of those also seen in aveALL).	Figure legend	Data can be extracted from Supplementary Table 2	NA	NA	NA
+ -	2b	None	NA	134	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Number of cis-eQTL signal per tissue	Figure legend	Data can be extracted from Supplementary Table 5	NA	NA	NA
+ -	3 (left panels)	None	NA	varies by tissue (N stated in axis)	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Boxplot of the expression data sorted by decreasing median values	Figure legend	None	NA	NA	NA
+ -	3 (right panels)	t-test on the linear regression coefficient for each SNP (additive model regressed on expression)	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	varies by tissue (N stated in axis)	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Boxplot of the expression data stratified by the genotype	Figure legend	10 p-values stated in Figure	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	N - 2 degrees of freedom	NA

+	-	4	t-test on the linear regression coefficient for each SNP (additive model regressed on expression)	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	varies by tissue	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Boxplot of the expression data stratified by the genotype	Figure legend	9 p-values stated in Figure	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	N - 2 degrees of freedom	NA
+	-	5a	t-test on the linear regression coefficient for each SNP (additive model regressed on expression)	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	130	all cerebellar cortex samples	Figure legend	boxplots - whiskers extend from the box to 1.5 times the inter-quartile range	Figure legend	5 p-values reported on the figure	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	N - 2 degrees of freedom	NA
+	-	5b	t-test on the linear regression coefficient for each SNP (additive model regressed on expression)	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	130	all cerebellar cortex samples	Figure legend	boxplots - whiskers extend from the box to 1.5 times the inter-quartile range	Figure legend	9 p-values reported on the figure	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	N - 2 degrees of freedom	NA
+	-	5c	two-sample Kolmogorov-Smirnov test	"The majority of cis-eQTL signals operate at the exon-level"	134	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Density plot of the two distribution	Figure legend	1.6e-10	"The majority of cis-eQTL signals operate at the exon-level"	non-parametric test	NA
+	-	5d	None	NA	NA	NA	NA	Enrichment ratio of each functional annotation category with respect to all tested variants	NA	NA	NA	NA	NA
+	-	6a	None	NA	These are made up of multiple 2x2 contingency tables.	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Enrichment ratio of variants with cis-eQTL vs all tested variants	Figure legend	None	NA	None	NA

+	6b	Fisher's exact test	NA	These are made up of multiple 2x2 contingency tables.	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Enrichment ratio of variants associated with internal cis-eQTL vs. external cis-eQTLs	Figure legend	p-value for UTR: 0.0026	Functional characterisation and localisation of cis-eQTL signals	NA	NA
+	7 (left panels)	t-test on the linear regression coefficient for each SNP (additive model regressed on expression)	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	varies by tissue	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	NA	NA	Multiple values plotted on -log <sub>10</sub> (P) scale	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	N - 2 degrees of freedom	NA
+	7 (right panels)	t-test on the linear regression coefficient for each SNP (additive model regressed on expression)	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	varies by tissue	all samples from all individuals	Online Methods "Collection and dissection of post-mortem human brain tissues"	Boxplot of the expression data stratified by the genotype	Figure legend	4 p-values stated in Figure	Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"	N - 2 degrees of freedom	NA

## ► Representative figures

- Are any representative images shown (including Western blots and immunohistochemistry/staining) in the paper?

If so, what figure(s)?

No

- For each representative image, is there a clear statement of how many times this experiment was successfully repeated and a discussion of any limitations in repeatability?

If so, where is this reported (section, paragraph #)?

Not applicable

## ► Statistics and general methods

- Is there a justification of the sample size?

If so, how was it justified?

Where (section, paragraph #)?

Even if no sample size calculation was performed, authors should report why the sample size is adequate to measure their effect size.

A post-hoc examination of the power to detect eQTL signals based on the sample size used is provided in Section "Replication of cis-eQTL signals in three independent datasets"

## 2. Are statistical tests justified as appropriate for every figure?

Where (section, paragraph #)?

Tests are described in Online Methods and justified if they are non-standard.

- a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined?

Yes - see Online Methods

- b. Do the data meet the assumptions of the specific statistical test you chose (e.g. normality for a parametric test)?

Where is this described (section, paragraph #)?

The t-test for eQTL association assumes normality of residuals from the linear model. We investigated assumption via comparison with permutation-based statistical testing, and found very good concordance between the two testing methods. See Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"

- c. Is there any estimate of variance within each group of data?

Is the variance similar between groups that are being statistically compared?

Where is this described (section, paragraph #)?

See 2a above

- d. Are tests specified as one- or two-sided?

A two-sided test is implicit in eQTL analysis. This is stated in the reference to the MatrixEQTL software. See Online Methods "Expression QTL analysis, FDR calculation and marker sentinelization"

- e. Are there adjustments for multiple comparisons?

Yes - We converted the nominal p-values into false discovery rates (FDR) using the Benjamini-Hochberg procedure. This was done separately for every combination of type of marker, type of expression level, cis or trans and tissue. We defined associations with resulting FDR < 1% as significant.

## 3. Are criteria for excluding data points reported?

Was this criterion established prior to data collection?

Where is this described (section, paragraph #)?

Yes - Data points were excluded based on quality control procedures applied to both our genotyping data and our expression data. The criteria for data exclusion based on genotyping information are reported in Online Methods, while those for expression data are reported in Tebbel *et al.* (2011), referenced in Online Methods.

## 4. Define the method of randomization used to assign subjects (or samples) to the experimental groups and to collect and process data.

If no randomization was used, state so.

Where does this appear (section, paragraph #)?

Genotypes assigned by Mendelian randomization. Brain regions assayed for all individuals where possible. Samples plated on an ad hoc basis.

## 5. Is a statement of the extent to which investigator knew the group allocation during the experiment and in assessing outcome included?

If no blinding was done, state so.

Where (section, paragraph #)?

Not applicable

## 6. For experiments in live vertebrates, is a statement of compliance with ethical guidelines/regulations included?

Where (section, paragraph #)?

Not applicable

7. Is the species of the animals used reported? Where (section, paragraph #)?	Not applicable
8. Is the strain of the animals (including background strains of KO/transgenic animals used) reported? Where (section, paragraph #)?	Not applicable
9. Is the sex of the animals/subjects used reported? Where (section, paragraph #)?	Yes - Supplementary Table 1
10. Is the age of the animals/subjects reported? Where (section, paragraph #)?	Yes - Supplementary Table 1
11. For animals housed in a vivarium, is the light/dark cycle reported? Where (section, paragraph #)?	Not applicable
12. For animals housed in a vivarium, is the housing group (i.e. number of animals per cage) reported? Where (section, paragraph #)?	Not applicable
13. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)? Where (section, paragraph #)?	Not applicable
14. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported? Where (section, paragraph #)?	Yes - We have only used samples from individuals who were neurologically normal during life and have neuropathologically normal brains. This is reported in Online Methods.
a. If multiple behavioral tests were conducted in the same group of animals, is this reported? Where (section, paragraph #)?	Not applicable
15. If any animals/subjects were excluded from analysis, is this reported? Where (section, paragraph #)?	3 individuals were removed from the sample set resulting in the analysis of samples taken from 134 individuals. This is described in Online Methods
a. How were the criteria for exclusion defined? Where is this described (section, paragraph #)?	Based on non-European ancestry as evidenced by the genetic data. This is described in Online Methods
b. Specify reasons for any discrepancy between the number of animals at the beginning and end of the study. Where is this described (section, paragraph #)?	As stated above 3 individuals were removed from the sample set resulting in the analysis of samples taken from 134 individuals as stated in the text.

## ► Reagents

1. Have antibodies been validated for use in the system under study (assay and species)?

Not applicable

- a. Is antibody catalog number given?

Not applicable

Where does this appear (section, paragraph #)?

- b. Where were the validation data reported (citation, supplementary information, Antibodypedia)?

Not applicable

Where does this appear (section, paragraph #)?

2. If cell lines were used to reflect the properties of a particular tissue or disease state, is their source identified?

Not applicable

Where (section, paragraph #)?

- a. Were they recently authenticated?

Not applicable

Where is this information reported (section, paragraph #)?

## ► Data deposition

Data deposition in a public repository is mandatory for:

- Protein, DNA and RNA sequences
- Macromolecular structures
- Crystallographic data for small molecules
- Microarray data

Deposition is strongly recommended for many other datasets for which structured public repositories exist; more details on our data policy are available [here](#). We encourage the provision of other source data in supplementary information or in unstructured repositories such as [Figshare](#) and [Dryad](#).

1. Are accession codes for deposit dates provided?

Yes. See section "Data availability and website"

Where (section, paragraph #)?

## ► Computer code/software

Any custom algorithm/software that is central to the methods must be supplied by the authors in a usable and readable form for readers at the time of publication. However, referees may ask for this information at any time during the review process.

1. Identify all custom software or scripts that were required to conduct the study and where in the procedures each was used.

Not applicable

2. Is computer source code/software provided with the paper or deposited in a public repository? Indicate in what form this is provided or how it can be obtained.

Not applicable

## ► Human subjects

- |                                                                                                                                                         |                                                                                                                                |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| <p>1. Which IRB approved the protocol?<br/>Where is this stated (section, paragraph #)?</p>                                                             | National Hospital for Neurology and Neurosurgery and Institute of Neurology Research Ethics Committee, Queen Square, London UK |
| <p>2. Is demographic information on all subjects provided?<br/>Where (section, paragraph #)?</p>                                                        | Yes - Supplementary Table 1                                                                                                    |
| <p>3. Is the number of human subjects, their age and sex clearly defined?<br/>Where (section, paragraph #)?</p>                                         | Yes - Supplementary Table 1                                                                                                    |
| <p>4. Are the inclusion and exclusion criteria (if any) clearly specified?<br/>Where (section, paragraph #)?</p>                                        | Yes - Online Methods                                                                                                           |
| <p>5. How well were the groups matched?<br/>Where is this information described (section, paragraph #)?</p>                                             | Not applicable                                                                                                                 |
| <p>6. Is a statement included confirming that informed consent was obtained from all subjects?<br/>Where (section, paragraph #)?</p>                    | Yes - Online Methods                                                                                                           |
| <p>7. For publication of patient photos, is a statement included confirming that consent to publish was obtained?<br/>Where (section, paragraph #)?</p> | Not applicable                                                                                                                 |

## ► fMRI studies

For papers reporting functional imaging (fMRI) results please ensure that these minimal reporting guidelines are met and that all this information is clearly provided in the methods:

- |                                                                                                                                             |                |
|---------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| <p>1. Were any subjects scanned but then rejected for the analysis after the data was collected?</p>                                        | Not applicable |
| <p style="padding-left: 20px;">a. If yes, is the number rejected and reasons for rejection described?<br/>Where (section, paragraph #)?</p> | Not applicable |
| <p>2. Is the number of blocks, trials or experimental units per session and/or subjects specified?<br/>Where (section, paragraph #)?</p>    | Not applicable |
| <p>3. Is the length of each trial and interval between trials specified?</p>                                                                | Not applicable |

4. Is a blocked, event-related, or mixed design being used? If applicable, please specify the block length or how the event-related or mixed design was optimized.	Not applicable
5. Is the task design clearly described?  Where (section, paragraph #)?	Not applicable
6. How was behavioral performance measured?	Not applicable
7. Is an ANOVA or factorial design being used?	Not applicable
8. For data acquisition, is a whole brain scan used?  If not, state area of acquisition.	Not applicable
a. How was this region determined?	Not applicable
9. Is the field strength (in Tesla) of the MRI system stated?	Not applicable
a. Is the pulse sequence type (gradient/spin echo, EPI/spiral) stated?	Not applicable
b. Are the field-of-view, matrix size, slice thickness, and TE/TR/flip angle clearly stated?	Not applicable
10. Are the software and specific parameters (model/functions, smoothing kernel size if applicable, etc.) used for data processing and pre-processing clearly stated?	Not applicable
11. Is the coordinate space for the anatomical/functional imaging data clearly defined as subject/native space or standardized stereotaxic space, e.g., original Talairach, MNI305, ICBM152, etc? Where (section, paragraph #)?	Not applicable
12. If there was data normalization/standardization to a specific space template, are the type of transformation (linear vs. nonlinear) used and image types being transformed clearly described? Where (section, paragraph #)?	Not applicable
13. How were anatomical locations determined, e.g., via an automated labeling algorithm (AAL), standardized coordinate database (Talairach daemon), probabilistic atlases, etc.?	Not applicable
14. Were any additional regressors (behavioral covariates, motion etc) used?	Not applicable
15. Is the contrast construction clearly defined?	Not applicable
16. Is a mixed/random effects or fixed inference used?	Not applicable

a. If fixed effects inference used, is this justified?	Not applicable
17. Were repeated measures used (multiple measurements per subject)?	Not applicable
a. If so, are the method to account for within subject correlation and the assumptions made about variance clearly stated?	Not applicable
18. If the threshold used for inference and visualization in figures varies, is this clearly stated?	Not applicable
19. Are statistical inferences corrected for multiple comparisons?	Not applicable
a. If not, is this labeled as uncorrected?	Not applicable
20. Are the results based on an ROI (region of interest) analysis?	Not applicable
a. If so, is the rationale clearly described?	Not applicable
b. How were the ROI's defined (functional vs anatomical localization)?	Not applicable
21. Is there correction for multiple comparisons within each voxel?	Not applicable
22. For cluster-wise significance, is the cluster-defining threshold and the corrected significance level defined?	Not applicable

## ► Additional comments

Additional Comments

None